buffering agents, solubilizing agents, tonicifying agents, antimicrobials and collapse temperature modifiers. *See* Table IV.[37]

Permeability enhancers

As well as poor solubility, a further factor that may prevent absorption of APIs is poor permeability. APIs may be poorly permeable if the molecule weight is very large (such as in the case of proteins and peptides) making the API too large to pass through the intercellular tight junctions in the intestinal wall. A further cause of poor permeability may be the presence of significant hydrogen bonding between API molecules, or if the API is highly hydrophobic.[38] No true permeability enhancers are included within oral solid dosage forms as excipients. Nevertheless, various different types of excipient may act as permeability enhancers by enhancing API transit through the intercellular tight junctions. Care must be taken if attempting to enhance permeability that the intestinal wall is not damaged.

Mechanisms by which excipients may improve permeability include membrane modulators, tight junction modulators, substrates of uptake transporters, carriers across membranes and inhibitors of efflux transporters as described by Hamman and Steenekamp.[39] Lipid excipients are a major class of permeability enhancers, which may also act to increase the solubility of hydrophobic APIs. Examples of lipid excipients include fatty acids, natural oils and fats, semisynthetic mono-, di- and triglycerides, semisynthetic polyethylene glycol (PEG) derivatives of glycerides and fatty acids, polyglyceryl fatty acid esters, cholesterols, phospholipids as well as ionic and nonionic surfactants.[40] The majority of lipid excipients are liquids at room temperatures and therefore for oral solid dosage forms may only be suitable for incorporation into soft or hard gelatin capsules. However, some solid lipids may be incorporated into tablets or powder in capsule (PIC) formulations. As well as promoting solubility and permeability, the incorporation of lipids may produce self-emulsifying drug delivery systems (SEDDS), promote supersaturation, increase gastrointestinal residence time, effect intestinal based efflux, and influence drug metabolism in the intestine.[41] Medium chain fatty acids such as capric acid, lauric acid, and their sodium salts, which are solid at room temperature, have been used as permeability enhancers although the biological mechanism by which they operate is still disputed.[42]

Surfactants

In order to further improve the bioavailability of an API within an oral solid dosage form a surfactant may also be included within the formulation. In the formulation of drug products, surfactants are commonly used as emulsifiers, solubilizers and wetting agents.[43] Surfactants may be broadly divided into anionic, cationic, amphoteric, and nonionic subgroups.

Anionic surfactants have a negative charge on the hydrophilic headgroup group which commonly consists of carboxylate, sulfate or sulfonate ions. Examples of the types of anions used include stearates, sulfosuccinates, lauryl sulfates, oleates and fumarates. Metal cations which are typically employed to balance the anionic charge include sodium, magnesium, calcium and zinc. Cationic surfactants have a positive charge on the hydrophilic headgroup and are generally considered to have a greater toxicity than anionic surfactants; therefore cationic surfactants are less commonly used. Examples of cationic surfactants include benzalkonium choride and cetrimide. Amphoteric surfactants have the ability to be positively charged, negatively charged, or neutral, depending on the pH of the media which they are in and are commonly found in cosmetics, but not oral solid dosage forms. Nonionic surfactants which may be used in oral solid dosage forms are numerous and include glycol and glycerol esters, sorbitan derivatives, polyoxyl esters, polyoxyl ethers, poloxamers, and natural emulsifiers (including phospholipids). Comprehensive lists may be found in the United States and European Pharmacopeias and are summarized by Marti-Mestres and Nielloud.[43]

Excipients used in Film Coating

Sometimes APIs are bitter in taste which may result in poor patient compliance when formulated within oral solid dosage forms. In addition, stability of the API may be compromised due to moisture ingress into the tablet core or exposure to light hence reducing shelf life. Film coating of tablets is therefore often performed in order to provide taste-masking of the formulation and to enhance stability.[44] Film coatings are also commonly used for decorative purposes in order to provide a color for the dosage form, thus providing a commercial image.

Typically, film coatings are applied by spraying an aqueous or organic solution of a polymer, a plasticizer (such as triacetin or polyethylene glycol) and if required an anti-tacking agent (such as talc) onto tablet cores which are then dried to remove the solvent. Various polymers are used for film coating, examples of which are shown in Table V.[44] For decorative film coats, hypromellose or polyvinyl alcohol are commonly used and globally acceptable pigments such as iron oxides or lakes may also be included to provide color to the tablets thus providing brand enhancement. In addition, the inclusion of certain polymers within a film coat may also be used to produce modified-release formulations.

It is advisable to ensure that dosage forms to be film coated do not contain excessive amounts of disintegrant (<5%) so that film defects or core erosion do not occur during the coating process. It is also advisable to keep lubricant levels below 2% in order to ensure suitable film adhesion to the core.

Modified release oral solid dosage forms

Modified-release formulations are used to modify the rate, place or time of drug release from a dosage form.

(a) Modifying the rate of drug release

Modified release products that affect the rate of drug release prolong drug absorption resulting in a longer time to maximum plasma concentration (t_{max}) and a lower maximum plasma concentration (C_{max}). This may allow for a reduction in the dosing

Table V: Polymers used for film coating oral solid dosage forms.

Water soluble polymers	Entero-soluble cationic polymers	Enteric, anionic polymers	Water insoluble polymers
Hydroxyethyl cellulose	Amino dimethyl methacrylate copolymer	Sodium alginate	Ethylcellulose
Hypromellose	Amino diethyl methacrylate copolymer	Shellac	Cellulose acetate
Carboxymethylcellulose sodium		Cellulose acetate phthalate	Poly (ethyl acrylate-co-methyl-methacrylate)
Povidone		Cellaburate	Ammonio methacrylates
Polyvinyl alcohol		Methacrylic acid copolymer (Types A, B and C)	Polyvinyl acetate
			Carboxymethylcellulose